Remarks/Arguments

Applicants' claims have been amended so that all claims not currently under consideration have been shown as cancelled. Applicants consider the claims presently under consideration to be 1-4, 8-13, 16-19, 22-27, 29-30, 33-39, 42-46, 49-50 and 53.

The Examiner has stated in paragraph 2, page 4, of the Office Action that the numbering of claims is not in accordance with 37 CFR 1.126. The Examiner then proceeds to state that all claims subsequent to claim 28 have been renumbered. This appears to be diametrically opposite the directions of 37 CFR 1.126, which states tha, "The original numbering of the claims must be preserved throughout the prosecution." The mere fact that a claim is missing does not constitute a reason for proceeding in violation of the directions of 37 CFR 1.126. Accordingly, Applicants have not renumbered the claims and submit that it is improper to do so. In the event that the Examiner wishes to renumber the claims, Applicants have no objection to his doing so, but Applicants consider this action to be in violation of the applicable law, as stated above.

To facilitate reference between the claims as originally numbered which remain in the application, the following listing is provided.

Claims finally rejected by Examiner in the Office Action dated March 1, 2007:

Applicants' listing – 1-5, 8-13, 16-19, 24-27, 29-30, 33-39, 42-46 and 49-50.

Examiner's listing – 1-5, 8-13, 16-19, 24-29, 32-38, 41-45, and 48-49.

Claims pending after entry of this Amendment:

Applicants' listing – 1-3, 8-13, 16-19, 24-27, 29-30, 33-35, 42-46 and 49-50.

Examiner's listing – 1-3, 8-13, 16-19, 24-29, 32-34, 41-45, and 48 -49.

The above lists illustrates the confusion resulting from renumbering claims contrary to 37 C.F.R. 1.126.

The objection to the disclosure because of the formalities listed in paragraph 1 on page 3 is noted. It is believed that these objections have been obviated by the amendments to Applicants' specification in paragraphs [0032], [0033], [0050], [0051] and [0081]. It is respectfully submitted that no one skilled in the art would be confused by the nomenclature

used by Applicants, but based upon the Examiner's objection, these paragraphs have been revised.

With respect to the objection to claim 28, this claim has been cancelled even though it was not initially presented. As discussed above, Applicants have not renumbered the remaining claims but have no objection to the Examiner's doing so if it is clearly done by the Examiner at the Examiner's own election.

The withdrawal of the objection to claim 29 is acknowledged with appreciation.

The objection to Applicants' claims 4, 13, and 46 is considered obviated by the cancellation of claim 4 to expedite prosecution, the amendment of claim 13 to supply a conjunction and with an amendment to claim 46 by underlining the word "contains."

The discussion of double patenting is noted but the requirement for a Terminal Disclaimer is respectfully traversed. With respect to this case, a restriction requirement was previously required and made by the Examiner under 35 U.S.C. 121, which provides that if two or more "independent and distinct inventions" are claimed in the application the Director may require the application to be restricted to one of the inventions. Since the Examiner concluded that there were separate and distinct inventions, it is difficult to see why a Terminal Disclaimer is now required. Further, it is pointed out that the claims do not overlap since the claims in U.S. Serial No. 11/442,907 are directed to a carrier with the claims in this application being directed to a carrier and a specific drug. Since these inventions were previously found by the Examiner to be separate and distinct, it is not clear why this obviousness double patenting rejection has been made. It is also noted in 35 U.S.C. 121 that a parent case cannot be applied against a divisional case. Nevertheless, since there is little disadvantage to Applicants to making the Terminal Disclaimer, a Terminal Disclaimer is attached hereto. It is believed that this obviates all rejections based upon the ground of non-statutory obviousness-double patenting.

The rejection of claims 34-38, 41-45 and 48-49 (Examiner's numbering) under 35 U.S.C. 112, first paragraph, is respectfully traversed and reconsideration is respectfully requested. Applicants have reviewed 35 U.S.C. 112, first paragraph, and are unable to find any requirement in this paragraph that "all possible formulations" be shown. The requirement is simply that the invention must be disclosed in such full, clear, concise and

exact terms as to enable any person skilled in the art to which it pertains, with which it is most closely connected, to make and use the same. The best mode known to Applicants is disclosed in the examples presently pending.

Further it is presumed that the Examiner is aware of the case authority which holds that it is sufficient if the application enables a determination that the inventor was in the possession of the invention at the time of filing; such as, for instance, *Ralston Purina Co. vs. Far-Mar Co., Inc, 227 USPQ 177,179 (Fed.Cir.1985).*

It is respectfully submitted that the specification does enable a person skilled in the art to make and use the invention. The Examiner's further discussion that the skepticism raised in the enablement rejection is that raised in the art by artisans of expertise does not appear to be supported by anything beyond the Examiner's opinion. No examples of this are given.

When a broad invention is disclosed and claimed, there is no reason that a broad patent should not issue. For instance, consider U.S. Patent 6,197,333 issued March 6, 2001 to Onyuksel et al, (herein Onyuksel) cited with apparent approval. This reference with showings limited to "biologically active amphipathic peptides, which are members of the family of peptide compounds, including vasoactive intestinal peptide (VIP) and growth hormone releasing factor (GRF)" was issued claims reciting the particular steps for producing the desired combination of lipids and then recites incubating these lipids with a biologically active amphipathic compound. This claim is far beyond the enablement shown in Onyuksel and is not limited to the specific peptide shown. It is respectfully submitted that Onyuksel does not show this broader range of materials at all except for one member which is shown in the specification.

It is respectfully submitted that Applicants have shown the use of the carrier with a drug. Not only are the claims now limited to the single drug but, as disclosed in the specification, that drug is encapsulated in the carrier (paragraph [0044]). This leads to the conclusion that the carrier is effective to deliver the drug and no serious question has been raised as to this disclosure. The remaining conjecture with respect to the state of the art, etc. is noted. However, it is respectfully submitted that none of this is relevant to the issue as to

whether one skilled in the art is able to duplicate Applicants' claimed invention. The examples show the preparation of the carrier encapsulated drug.

Regarding the Examiner's comments with respect to Applicants' arguments, the Examiner has stated "Applicant has missed the point the Examiner is trying to make, specifically the inability to reasonably extrapolate to the larger genus of liposome formations of diverse component compositions encompassed by the claims based upon a single liposome example. The drug carried by the liposome is immaterial to the enablement rejection." It is difficult to understand how if the drug is immaterial, the Examiner has restricted this application to a single drug. Further it is disclosed in the application that the liposomes are tailored to be compatible with naturally-occurring fluids in the lung of the mammal. This information is available to those skilled in the art and would certainly enable those skilled in the art to produce liposomes useful in the carriers of the present invention.

The Examiner's difficulty in finding support of the instant specification for the limitations of parent claims 3-5 is difficult to understand. Particularly, please note with respect to claim 3, which requires that the carrier contain up to 50 percent phosphatidylcholine, that the phosphatidylcholine may comprise the only head group. This certainly includes at least 50 percent.

The difficulty with respect to claim 8 is hard to understand in view of paragraph [0028]. Also, the difficulty with respect to the support for claims 9 and 10 considering that these claims as originally filed contain the limitations of carbon number ranges of 8-18 and 16- 18. It appears that the Examiner is grasping at straws to find some basis for rejection.

Upon review of the specification, in view of these claims, it is believed that many of the Examiner's objections will disappear.

The rejection of Applicants' claims 8 and 25 under 35 U.S.C. 112 has been obviated by Applicants' actions with respect to these claims. The Examiner maintains his rejection of claims 3-5, 23-26, 35 and 52.

Claim 5 is not considered by Applicants to currently be in prosecution.

With respect to the Examiner's difficulties with claims 23 -26, please note that the material in claim 22 appears to be originally filed material except for an amendment to depend from claim 18. This claim requires that the phosphatidylcholine is present in an

amount from about 50 to about 100 percent, which certainly is supported by the language at paragraph [0026].

Claim 23 requires that the carrier include up to about 50 weight percent phosphatidylglycerol. This is also hard to consider unsupported in view of paragraph [0027]. With respect to claims 25 and 26, see paragraphs [0028] and [0029].

With respect to claim 35, it is believed that this objection has been previously addressed. If not, please see paragraph [0026].

Claim 52 has been cancelled.

The rejection of Applicants' claims 1, 5, 8-13 and 16-17 under 35 U.S.C. as anticipated by Onyuksel is respectfully traversed and reconsideration is respectfully requested.

In view of the Examiner's position to the effect that each drug is a separate invention, it is difficult to see how any rejection can be made under Onyuksel. Onyuksel does not relate to the use of budesonide, which is required in all of Applicants' claims. Onyuksel does not show any method for using a carrier, such as claimed by Applicants, to encapsulate budesonide or any other drug for inhalational therapy. Onyuksel's compositions are used intravenously and do not provide any substantial extended effectiveness for the drug. Onyuksel discloses a method of preparation at column 16, lines 18-38 which is not contemplated by Onyuksel's disclosure where a drug was initially mixed with a lipid composition followed by extrusion and repeated freezing and thawing to produce liposomes. This method is disclosed to be non-preferred and ineffective to elicit an increase (column 17, lines 42-43). Onyuksel also compares this material as not effective as were the Onyuksel materials (column 17, lines 49-50) and states at column 17 that "SSL in general are not amenable to the present invention."

Onyuksel does not disclose the use of the drug used by Applicants. It does not disclose the use of a carrier encapsulating a drug as described by Applicants. It does not describe the use of the drug. It does not show, enable or suggest the use of the carrier with the drug in mammalian lungs and in no way shows or suggest Applicants' claimed invention. It is respectfully requested that these objections be withdrawn.

It is noted that the Examiner comments in his response to Applicants arguments that "The drug is not germane to claims drawn to the liposome carrier composition." This is a startling statement considering that the invention was narrowly restricted to a single drug. It is not clear whether the Examiner considers the drug to be completely immaterial and not germane or whether he considers it to be a basis for restriction. Since the restriction has already been made, it is respectfully pointed out that Onyuksel does not use the same drug, does not use a drug in the same way and discloses that the method used for producing the carrier used by Applicants is ineffective and does not elicit the desired response. It is difficult to see how this reference can be considered effective to show or suggest Applicants' claimed invention.

The rejection of Applicants' claims 1-2, 5, 8-13, 16-17 and 52 as unpatentable in view of Onyuksel, Waldrep, et al and Konduri, et al. is respectfully traversed and reconsideration is respectfully requested. Claims 5 and 52 have been cancelled.

The Examiner has asserted that Onyuksel shows that polymers known and routinely used in the art of sterically stabilized liposome technology are as described below. The Examiner correctly acknowledged that Onyuksel does not disclose that the disclosed liposome formulations do not extend the life of the drug by at least two or three times the drug life alone. Onyuksel also does not disclose the use of or any system for achieving use of the drugs with the liposome carrier in the lungs. All of the applications disclosed in Onyuksel are intravenous. Further different drugs are used and there is no suggestion of how the drugs might be administered to the lungs. The Examiner also acknowledges that Onyuksel does not explicitly teach phosolipids which applicant requires. This could be because Onyuksel is using the phosolipids intravenously, whereas Applicants use them in the lungs.

Waldrep, et al, U.S. Patent 5,958,378 issued September 28, 1999 (herein Waldrep) has been cited as disclosing the use of a formulation of liposome carrying budesonide wherein other phosolipids might be substituted for DLPC. It is not suggested that Waldrep shows the use of stabilized liposomes. Applicants have shown in the examples that sterically stabilized liposomes with the drug obtain the extended life but that non-sterically stabilized

liposomes do not. Therefore, Waldrep simply shows a proposed technique which has been shown not to work in Applicants' application.

The Examiner, after having concluded that the disclosures of the Applicants are not sufficient to enable those skilled in the art, has now jumped to the conclusion that it would now be obvious to one skilled in the art to modify sterically stabilized liposomes of Onyuksel to comprise other phosolipids, etc. It is also been suggested that Applicants acknowledged in the paper filed December 11, 2006 that the method of making stabilized liposomes was well known. While this may be so, there is no suggestion that it is known to make sterically stabilized liposomes which are effective as Applicants' carrier.

No suggestion was noted in any of the references which would lead those skilled in the art to attempt to develop Applicants' claimed invention.

The rejection of Applicants' claims 18-19, 22-27, 28-29, 32-38, 41-45 and 48-49 under 35 U.S.C. 103 is respectfully traversed and reconsideration is respectfully requested. These claims are directed to a composition, the carrier and budesonide and to methods for using the composition. These claims are rejected in view of Konduri, et al, in view of Onyuksel and Waldrep. Since these references do not show or suggest the composition, it is difficult to see how they can be considered to show or suggest a composition and method representing the carrier, plus drug, in the composition and for use in treatment. It is respectfully submitted that nothing in these references shows or suggests either the carrier, encapsulating a drug, or a method for treating the lungs of a mammal by the use of the carrier. Particularly, there is no showing in any of these references of the stabilized liposomes to be used or the applicable dosages or the methods for administration. The Examiner's conclusion that these claims are obvious is respectfully traversed and reconsideration is respectfully requested.

It is considered that the foregoing comments are responsive to all issues raised in the Office Action. It is further submitted that none of Applicants' claims, as amended, are now objectionable and that all rejections of Applicants' claims under 35 U.S.C. 112 have been obviated.

Accordingly, it is respectfully requested that all rejections of Applicants' claims under 35 U.S.C. 112 be withdrawn.

It is also submitted that in view of the foregoing amendments and comments that none of Applicants' claims have been shown or suggested under 35 U.S.C. 102 or 35 U.S.C. 103 by any of the applied references, taken alone or in combination.

Since Applicants' claims are now considered in condition for allowance, such is respectfully solicited.

Entry of this amendment is respectfully requested since it substantially reduces the number of claims, reduces the number of issues and is considered to place Applicant's claims in condition for allowance or in better condition for appeal.

Respectfully submitted,

F. Lindsey Scott

F. Lindsey Scott
Registration No. 26,230
972.599.2888
Attorney for Applicants

2329 Coit Road
Suite B
Plano, TX 75075-3796